

In the Specification:

Compliance with 37 C.F.R. § 1.821, *et seq.*, herein, necessitates the following amendment be made to the specification. In this amendment, please amend the paragraph sections noted below. The text to be amended has been placed between ellipses (...). Where the text to be amended is located at the beginning or the ending of a paragraph, ellipses will not be used.

Beginning with ¶ No. [0021], please amend the paragraphs in the specification as follows:

[0021] ... a C-terminal sequence consisting of KPV (SEQ ID NO: 1), HFRWGKPV (SEQ ID NO: 2), and SYSMEHFRWGKPV (SEQ ID NO: 3) ...

[0025] ... KPV (SEQ ID NO: 1) or VPK-Ac-CC-Ac-KPV (SEQ ID NO: 4)  
(Ac=Acetyl group)...

[0026] ... KPV (SEQ ID NO: 1), HFRWGKPV (SEQ ID NO: 2), and  
SYSMEHFRWGKPV (SEQ ID NO: 3) is topically ...

[0028] ... invention, ~~one or~~ one or more peptides selected from the group of  
peptides with a C-terminal sequence consisting of KPV (SEQ ID NO: 1), HFRWGKPV  
(SEQ ID NO: 2), and SYSMEHFRWGKPV (SEQ ID NO: 3), which may ...

[0029] Figure 1 illustrates the effect of  $\alpha$ -MSH (1-13) (SEQ ID NO: 3) and (11-13)  
(SEQ ID NO: 1) and the peptide VPK-Ac-CC-Ac-KPV (SEQ ID NO: 4) on *C. albicans*  
colony ...

[0030] ...  $\alpha$ -MSH (1-13) (SEQ ID NO: 3), (6-13) (SEQ ID NO: 2), and (11-13)  
(SEQ ID NO: 1).

[0033] ...  $\alpha$ -MSH (1-13) (SEQ ID NO: 3) treatment ...

- [0034] ...  $\alpha$ -MSH (11-13) (SEQ ID NO: 1) treatment ...
- [0035] ...  $\alpha$ -MSH (1-13) (SEQ ID NO: 3) and (11-13) (SEQ ID NO: 1) on ...
- [0036] ...  $\alpha$ -MSH (1-13) (SEQ ID NO: 3), (11-13) (SEQ ID NO: 1), and ...
- [0037] ...  $\alpha$ -MSH (1-13) (SEQ ID NO: 3), (11-13) (SEQ ID NO: 1), and ...
- [0038] ...  $\alpha$ -MSH (11-13) (SEQ ID NO: 3) relative to ...
- [0039] ...  $\alpha$ -MSH(11-13) (SEQ ID NO: 1) of inflammation ...
- [0040] ... by Ac-[D-Lys<sup>11</sup>] $\alpha$ -MSH(11-13)-NH<sub>2</sub> (SEQ ID NO: 5). Scores ...
- [0041] ... by Ac-[D-Pro<sup>12</sup>] $\alpha$ -MSH(11-13)-NH<sub>2</sub> (SEQ ID NO: 6). Scores ...
- [0042] ... by Ac-[D-Val<sup>13</sup>] $\alpha$ -MSH(11-13)-NH<sub>2</sub> (SEQ ID NO: 7). Scores ...
- [0043] ... by Ac-[D-Lys<sup>11</sup>, D-Val<sup>13</sup>] $\alpha$ -MSH(11-13)-NH<sub>2</sub> (SEQ ID NO: 8). Scores ...
- [0044] ...  $\alpha$ -MSH(11-13)'s (SEQ ID NO: 1) anti-inflammatory ...
- [0045] ... administered  $\alpha$ -MSH(11-13) (SEQ ID NO: 1) by ...
- [0046] ...  $\alpha$ -MSH(11-13) (SEQ ID NO: 1) in the presence ...
- [0047] ...  $\alpha$ -MSH(11-13) (SEQ ID NO: 1) as a ...
- [0048] ...  $\alpha$ -MSH(11-13) (SEQ ID NO: 1) as a ...
- [0049] ...  $\alpha$ -MSH(11-13) (SEQ ID NO: 1) as a ...
- [0050] ...  $\alpha$ -MSH(11-13) (SEQ ID NO: 1) concentration ...
- [0051] ...  $\alpha$ -MSH(1-13) (SEQ ID NO: 3) concentration ...
- [0052] ... ACTH (1-24) (SEQ ID NO: 12) concentration ...
- [0053] ...  $\alpha$ -MSH(1-13) (SEQ ID NO: 3) and  $\alpha$ -MSH(11-13) (SEQ ID NO: 1) concentration ...
- [0054] ...  $\alpha$ -MSH(11-13) (SEQ ID NO: 1) microglia ....

- [0055] ... peptides (ACTH (1-24) (SEQ ID NO: 12),  $\alpha$ -MSH(1-13) (SEQ ID NO: 3),  $\alpha$ -MSH(11-13) (SEQ ID NO: 1)) on TNF- $\alpha$  ...
- [0056] ... KPV peptide (SEQ ID NO: 1), KPV dimer (SEQ ID NO: 4) and ...
- [0057] ...  $\alpha$ -MSH (SEQ ID NO: 3) is a 13 amino acid, anti-inflammatory, anti-fugal peptide with the primary sequence SYSMEHFRWGKPV (SEQ ID NO: 3). In addition to its anti-fungal, anti-inflammatory properties, it also has anti-pyretic properties. The C-terminal trimer, KPV (SEQ ID NO: 1), appears ...
- [0058] The core  $\alpha$ -MSH sequence (4-10) (SEQ ID NO: 10) has ...
- [0059]  $\alpha$ -MSH (SEQ ID NO: 3) is produced by the post translational processing of propiomelanocortin and shares the 1-13 primary sequence with adrenocortitrophic hormone (ACTH) (SEQ ID NO: 9) ...
- [0061] ... consisting of KPV (SEQ ID NO: 1), HFRWGKPV (SEQ ID NO: 2), and SYSMEHFRWGKPV (SEQ ID NO: 3) in combination ...
- [0062] ... consisting of KPV (SEQ ID NO: 1), HFRWGKPV (SEQ ID NO: 2), and SYSMEHFRWGKPV in combination ...
- [0065] ... VPK-Ac-CC-Ac-KPV (Ac=Acetyl group), ...
- [0066] ... KPV (SEQ ID NO: 1), HFRWGKPV (SEQ ID NO: 2), and SYSMEHFRWGKPV ...
- [0068] ... KPV (SEQ ID NO: 1), HFRWGKPV (SEQ ID NO: 2), and SYSMEHFRWGKPV (SEQ ID NO: 3), ....
- [0069] ... KPV (SEQ ID NO: 1), HFRWGKPV (SEQ ID NO: 2), and SYSMEHFRWGKPV (SEQ ID NO: 3), which ...
- [0070] The following examples teach the utility of  $\alpha$ -MSH  $\alpha$ -MSH as ...

[0071] The peptides used in the following examples include:  $\alpha$ -MSH (1-13) (SEQ ID NO: 3), (4-10) (SEQ ID NO: 10), (6-13) (SEQ ID NO: 2), and (11-13) (SEQ ID NO: 1), all of which were N-acetylated and C-amidated, and ACTH (1-39) (SEQ ID NO: 9), and (18-39) (SEQ ID NO: 11) (CLIP)... KPV (SEQ ID NO: 1), VPK-Ac-CC-Ac-KPV (SEQ ID NO: 4), which also was N-acetylated and C-amidated (KPV dimer) ...

[0074] Example 1 suggests that  $\alpha$ -MSH (11-13) (SEQ ID NO: 1), (6-13) (SEQ ID NO: 2) and (1-13) (SEQ ID NO: 3) exhibit s...that  $\alpha$ -MSH (11-13) (SEQ ID NO: 1), (6-13) (SEQ ID NO: 2) and (1-13) (SEQ ID NO: 3) may ...

[0075] ...  $\alpha$ -MSH (1-13) (SEQ ID NO: 3) or (11-13) (SEQ ID NO: 1) at concentrations ...

[0076] ...  $\alpha$ -MSH (4-10) (SEQ ID NO: 10), (6-13) (SEQ ID NO: 2), (11-13) (SEQ ID NO: 1), ACTH (1-39) (SEQ ID NO: 9), (18-39) (SEQ ID NO: 11) and ...

[0077} ...  $\alpha$ -MSH (1-13) (SEQ ID NO: 3) and (11-13) (SEQ ID NO: 1)...VPK-Ac-CC-Ac-KPV (SEQ ID NO: 4) peptide ...

[0078] ...  $\alpha$ -MSH (11-13) (SEQ ID NO: 1), (6-13) (SEQ ID NO: 2), and (1-13) (SEQ ID NO: 3) were ...  $\alpha$ -MSH sequence (4-10) (SEQ ID NO: 10), which ...  $\alpha$ -MSH fragments bearing the KPV signal sequence, i.e.,  $\alpha$ -MSH (6-13) (SEQ ID NO: 2) and (11-13) (SEQ ID NO: 1) (p<.01), or the parent molecule  $\alpha$ -MSH (1-13) (SEQ ID NO: 3), (p<.05). ACTH (1-39) (SEQ ID NO: 9) and the ACTH fragment (18-39) (SEQ ID NO: 11) did not reduce *C. albicans* viability. Even higher concentrations of these ACTH (SEQ ID NO: 9) peptides ...

[0079] These results show that  $\alpha$ -MSH (1-13) (SEQ ID NO: 3), its C-terminal tripeptide (11-13) (SEQ ID NO: 1), and ... KPV of the  $\alpha$ -MSH  $\alpha$ -MSH sequence, i.e.,  $\alpha$ -MSH (1-13) (SEQ ID NO: 3), (6-13) (SEQ ID NO: 2), and (11-13) (SEQ ID NO: 1). In addition, the sequence VPK-Ac-CC-Ac-KPV (SEQ ID NO: 4) has also been shown to be at least as effective as  $\alpha$ -MSH (11-13) (SEQ ID NO: 1) against microbes. The  $\alpha$ -MSH core sequence (4-10) (SEQ ID NO: 10), which is known to influence learning and memory, but has little antipyretic and anti-inflammatory influence, was effective, but less so. The ACTH peptides (1-39) (SEQ ID NO: 9) and (18-39) (SEQ ID NO: 11) did not have significant candidacidal effects ...  $\alpha$ -MSH (SEQ ID NO: 3). This strongly suggests that  $\alpha$ -MSH (1-13) (SEQ ID NO: 3), its C-terminal tripeptide (11-13) (SEQ ID NO: 1), and other ...

[0080] Example 2 demonstrates that  $\alpha$ -MSH(1-13) (SEQ ID NO: 3) , (6-13) (SEQ ID NO: 2) or (11-13) (SEQ ID NO: 1) strongly inhibits Candidal germination. Accordingly, Example 2 also suggests that  $\alpha$ -MSH (1-13) (SEQ ID NO: 3) , (6-13) (SEQ ID NO: 2) or (11-13) (SEQ ID NO: 1) may be ...  $\alpha$ -MSH (1-13) (SEQ ID NO: 3), (6-13) (SEQ ID NO: 2) or (11-13) (SEQ ID NO: 1) at a ...

[0081] Figs. 3A-D show that coincubation of *C. albicans* with  $\alpha$ -MSH (1-13) (SEQ ID NO: 3) or (11-13) (SEQ ID NO: 1) inhibited germ tube formation induced by horse serum,  $\alpha$ -MSH (1-13) (SEQ ID NO: 3) caused 28-32% reduction in the number of filamentous cells; the tripeptide inhibited germination by 54-58%. The octapeptide  $\alpha$ -MSH (6-13) (SEQ ID NO: 2) had similar activity (approximately 50% inhibition)(not shown).

[0082] These results show that  $\alpha$ -MSH(1-13) (SEQ ID NO: 3),  $\alpha$ -MSH(6-13) (SEQ ID NO: 2), and  $\alpha$ -MSH(11-13) (SEQ ID NO: 1) all ...  $\alpha$ -MSH(1-13) (SEQ ID NO: 3) inhibited subsequent germ tube formation by approximately 30%,  $\alpha$ -MSH(11-13) (SEQ ID NO: 1) inhibited germ tube formation by approximately 56%, and  $\alpha$ -MSH (6-13) (SEQ ID NO: 2) inhibited ... KPV (SEQ ID NO: 1) amino acid sequence. The results of example 2 suggest that  $\alpha$ -MSH(1-13) (SEQ ID NO: 1), fragments of  $\alpha$ -MSH(1-13) (SEQ ID NO: 3) ...

[0083] Example 3 illustrates that  $\alpha$ -MSH (SEQ ID NO: 3) and its ...

[0084] ...  $\alpha$ -MSH (1-13) (SEQ ID NO: 3) or  $\alpha$ -MSH (11-13) (SEQ ID NO: 1) in ...

[0085] Fig. 4 shows that  $\alpha$ -MSH (1-13) (SEQ ID NO: 3) and (11-13) (SEQ ID NO: 1) enhanced ...

[0087] These results show that  $\alpha$ -MSH (1-13) (SEQ ID NO: 3) and  $\alpha$ -MSH (11-13) (SEQ ID NO: 1) do not ...

[0088] ...  $\alpha$ -MSH (1-13) (SEQ ID NO: 3), (11-13) (SEQ ID NO: 1), forskolin, ...

[0089] ...  $\alpha$ -MSH (1-13) (SEQ ID NO: 3) and (11-13) (SEQ ID NO: 1) enhanced cAMP ... by  $\alpha$ -MSH (SEQ ID NO: 3).

[0091] ...  $\alpha$ -MSH (1-13) (SEQ ID NO: 3) and  $\alpha$ -MSH (11-13) (SEQ ID NO: 1) both increased cAMP levels in *C. albicans*, with  $\alpha$ -MSH (11-13) (SEQ ID NO: 1) having the larger effect of the two. The increase in cAMP caused by  $\alpha$ -MSH (11-13) (SEQ ID NO: 1) was ... of  $\alpha$ -MSH(1-13) (SEQ ID NO: 3) and  $\alpha$ -MSH(11-13) (SEQ ID NO: 1). ... which  $\alpha$ -MSH (SEQ ID NO: 3) exerts ... that  $\alpha$ -MSH (SEQ ID NO: 3) exerts its ...

[0092] ... of  $\alpha$ -MSH (SEQ ID NO: 3) would ...

[0093] ... tripeptide Ac-Lys-Pro-Val-NH<sub>2</sub> (SEQ ID NO: 1) were ...

TABLE I

Anti-inflammatory Activity of the Tripeptide (SEQ ID NO: 1)

No Animals Tested	Tripeptide ( <u>SEQ ID NO: 1</u> ) Dose +	Result
3 (2E, 1C)	5	E lighter than C
2 (1E, 1C)	10	E lighter than C
2 (1E, 1C)	5	E lighter than C
2 (1E, 1C)	1.25	E lighter than C
2 (1E, 1C)	0.625	No difference observed

\*E = experimental; C = control

+ Dosages in ug of protected tripeptide per kg body weight, administered intravenously

[0094] ... tripeptide (SEQ ID NO: 1) per kg ...

[0095] These results show that a peptide containing the KPV (SEQ ID NO: 1) amino acid sequence of  $\alpha$ -MSH (SEQ ID NO: 3) has ... KPV (SEQ ID NO: 1) tripeptide, the histamine-induced weal exhibited a substantially less intense blue color. This suggests that the KPV (SEQ ID NO: 1) tripeptide is interfering with the ability of histamine to increase blood vessel permeability. ... the KPV tripeptide (SEQ ID NO: 1) to block histamine function suggests that peptides containing the  $\alpha$ -MSH KPV (SEQ ID NO: 1) ...

[0096] ...  $\alpha$ -MSH (SEQ ID NO: 3) may ... tripeptide (SEQ ID NO: 1) was ...

[0097] ... tripeptide (Ac-Lys-Pro-Val-NH<sub>2</sub>, (SEQ ID NO: 1) 100 mg/kg, N=6), of ...

[0099] These results show that a peptide containing the KPV (SEQ ID NO: 1) amino acid sequence of  $\alpha$ -MSH (SEQ ID NO: 3) could serve as a potential replacement for corticosteroids in the treatment of inflammation.  $\alpha$ -MSH (11-13) (SEQ ID NO: 1) was ... presence of  $\alpha$ -MSH (11-13) (SEQ ID NO: 1). Between 1 and 4 hours, however,  $\alpha$ -

MSH (11-13) (SEQ ID NO: 1) and ... suggested that the  $\alpha$ -MSH tripeptide (SEQ ID NO: 1) inhibits inflammation by blocking histamine function, example 6 suggests that  $\alpha$ -MSH (SEQ ID NO: 3) may also inhibit inflammation via a mechanism similar to that of the corticosteroids. It is also believed that  $\alpha$ -MSH (SEQ ID NO: 3) serves to inhibit inflammation by increasing the formation of endogenous corticosteroids. These substances are up-regulated by ACTH (SEQ ID NO: 9), which like  $\alpha$ -MSH (SEQ ID NO: 3) is a melanocortin peptide. Regardless of the exact mechanism of  $\alpha$ -MSH (SEQ ID NO: 3) anti-inflammatory activity, these results suggest that peptides containing the C-terminal  $\alpha$ -MSH amino acid sequence KPV (SEQ ID NO: 1) have potential therapeutic utility in the treatment of inflammation, particularly inflammation tied to sinusitis.

[0100] Example 7 suggests that  $\alpha$ -MSH (SEQ ID NO: 3) and its ... chirality tripeptide (SEQ ID NO: 1) can markedly affect the peptides  $\alpha$ -MSH (SEQ ID NO: 3) anti-inflammatory properties. ...

[0101] ... Ac- $\alpha$ -MSH (11-13)-NH<sub>2</sub> (SEQ ID NO: 1), i.e., Ac-Lys-Pro-Val-NH<sub>2</sub>) (SEQ ID NO: 1), Ac[D-Lys<sup>11</sup>]  $\alpha$ -MSH(11-13)-NH<sub>2</sub> (SEQ ID NO: 5), Ac[D-Pro<sup>12</sup>]  $\alpha$ -MSH(11-13)-NH<sub>2</sub> (SEQ ID NO: 6), Ac[D-Val<sup>13</sup>]  $\alpha$ -MSH(11-13- NH<sub>2</sub> (SEQ ID NO: 7), or Ac-[D-Lys<sup>11</sup>, D-Val<sup>13</sup>]  $\alpha$ -MSH(11-13)-NH<sub>2</sub> (SEQ ID NO: 8) in ...

[0104] Fig. 8 illustrates inhibition by  $\alpha$ -MSH (11-13) (SEQ ID NO: 1) of ... Ac- $\alpha$ -MSH(11-13)-NH<sub>2</sub> (SEQ ID NO: 1) inhibited acute inflammation ...

[0105] Fig. 9 illustrates that Ac[D-Lys<sup>11</sup>]  $\alpha$ -MSH(11-13)-NH<sub>2</sub> (SEQ ID NO: 5) ... that Ac [D-Pro<sup>12</sup>]  $\alpha$ -MSH(11-13)-NH<sup>2</sup> (SEQ ID NO: 6) had ... that Ac[D-Val<sup>13</sup>]  $\alpha$ -MSH(11-13)- NH<sub>2</sub> (SEQ ID NO: 7) had ...

[0106] As Fig. 12 illustrates, Ac-[D- Lys<sup>11</sup>, D-Val<sup>13</sup>]  $\alpha$ -MSH(11-13)-NH<sub>2</sub> (SEQ ID NO: 8) showed ...

[0107] ... Ac- $\alpha$ -MSH(11-13)-NH<sup>2</sup> (SEQ ID NO: 1) suggests that its actions rank roughly third among those recorded. The lack of significant effect on inflammation of the Ac [D-Pro<sup>12</sup>]  $\alpha$ -MSH(11-13)-NH<sub>2</sub> (SEQ ID NO: 6) indicates ...

[0108] ... Ac[D-Val<sup>13</sup>]  $\alpha$ -MSH(11-13)- NH<sub>2</sub> (SEQ ID NO: 7) and Ac-[D-Lys<sup>11</sup>, D-Val<sup>13</sup>]  $\alpha$ -MSH(11-13)-NH<sub>2</sub> (SEQ ID NO: 8) and reduced the anti-inflammatory activity in Ac[D-Pro<sup>12</sup>]  $\alpha$ -MSH(11-13)-NH<sub>2</sub> (SEQ ID NO: 6) .

[0109] These results again show the ability of the  $\alpha$ -MSH(11-13) (SEQ ID NO: 1) tripeptide ... peptide.  $\alpha$ -MSH(11-13) ...  $\alpha$ -MSH(11-13) (SEQ ID NO: 1) dosage, ...  $\alpha$ -MSH(11-13) (SEQ ID NO: 1) ...

[0111] ... animal.  $\alpha$ -MSH(1-13) (SEQ ID NO: 3) (1663.9 gm/mol; Peninsula Laboratories, Belmont, CA) or  $\alpha$ -MSH<sub>1-13</sub>  $\alpha$ -MSH(11-13) (SEQ ID NO: 1) ...

[0116] ...  $\alpha$ -MSH (1-13) (SEQ ID NO: 3) (inhibition by  $\alpha$ -MSH (SEQ ID NO: 3) was 36% ...  $\alpha$ -MSH (1-13)'s (SEQ ID NO: 3) anti-inflammatory ... the  $\alpha$ -MSH(1-13)'s (SEQ ID NO: 3) anti-inflammatory ... of  $\alpha$ -MSH (SEQ ID NO: 3). As is ... of  $\alpha$ -MSH (1-13) (SEQ ID NO: 3).

[0117] As shown in Fig. 16, central administration of  $\alpha$ -MSH (1-13) (SEQ ID NO: 3) in ... administered  $\alpha$ -MSH (1-13) (SEQ ID NO: 3). As ... effect of  $\alpha$ -MSH (1-13) (SEQ ID NO: 3) given intraperitoneally, there was a significant, although smaller, inhibitory effect later in the period.

[0118] ... signals,  $\alpha$ -MSH (1-13) (SEQ ID NO: 3) was ...

[0119] ...  $\alpha$ -MSH(1-13) (SEQ ID NO: 3) on IL-1 $\beta$ -induced ... effects of  $\alpha$ -MSH(1-13) (SEQ ID NO: 3). However, ... effectiveness of  $\alpha$ -MSH(1-13) (SEQ ID NO: 3). ... on  $\alpha$ -MSH(1-13) (SEQ ID NO: 3) activity, regardless ... injected  $\alpha$ -MSH(1-13) (SEQ ID NO: 3) exerts ...  $\alpha$ -MSH(1-13) (SEQ ID NO: 3) activity ... activity of  $\alpha$ -MSH(1-13) (SEQ ID NO: 3), ... anti-inflammatory effect of  $\alpha$ -MSH(1-13) (SEQ ID NO: 3).

[0120] The anti-inflammatory effect of  $\alpha$ -MSH (SEQ ID NO: 3) was next measured in mice with transected spinal cords. Centrally injected  $\alpha$ -MSH(1-13) (SEQ ID NO: 3) greatly ... Peripherally injected  $\alpha$ -MSH(1-13) (SEQ ID NO: 3), on the ... injected  $\alpha$ -MSH(11-13) (SEQ ID NO: 1) was even ... treated with  $\alpha$ -MSH(1-13) (SEQ ID NO: 3) ...

[0121] Example 9 suggests that the anti-inflammatory peptides of  $\alpha$ -MSH (SEQ ID NO: 3) may be ...

[0122] ... of  $\alpha$ -MSH (1-13) (SEQ ID NO: 3),  $\alpha$ -MSH (11-13) (SEQ ID NO: 1), and ACTH (1-24) (SEQ ID NO: 12) (Sigma) ...

[0125] ... (4)  $\alpha$ -MSH (1-13) (SEQ ID NO: 3) or  $\alpha$ -MSH (11-13) (SEQ ID NO: 1) (1, 10, 50  $\mu$ M); (5) LPS + IFN- $\gamma$  and either  $\alpha$ -MSH (1-13) (SEQ ID NO: 3) or  $\alpha$ -MSH (11-13) (SEQ ID NO: 1) (10  $\mu$ M). Reactions ...

[0127] ... peptides (ACTH (1-24) (SEQ ID NO: 11), ACTH (1-39) (SEQ ID NO: 9),  $\beta$ -MSH,  $\gamma$ -MSH) is <0.002%.

[0128] ...rabbit anti- $\alpha$ -MSH (SEQ ID NO: 3) produced by ...

[0130] As is shown in Fig. 19 micromolar concentrations of  $\alpha$ -MSH (1-13) (SEQ ID NO: 3) ...  $\alpha$ -MSH (1-13) (SEQ ID NO: 3) ... the preclusion production ...

microglia with  $\alpha$ -MSH (1-13) (SEQ ID NO: 3) and  $\alpha$ -MSH (11-13) (SEQ ID NO: 1) increased ...

[0131] ... peptides  $\alpha$ -MSH (1-13) (SEQ ID NO: 3),  $\alpha$ -MSH (11-13) (SEQ ID NO: 1) ACTH (1-24), (SEQ ID NO: 12) on TNF- $\alpha$  ...

[0132] ... with  $\alpha$ -MSH(1-13) (SEQ ID NO: 3),  $\alpha$ -MSH (11-13) (SEQ ID NO: 1), or ACTH(1-24) (SEQ ID NO: 12) prior to addition of LPS and IFN- $\gamma$  display a substantial decrease in production of TNF- $\alpha$ , IL-6, and NO.  $\alpha$ -MSH(1-13) (SEQ ID NO: 3) was most effective at inhibiting cytokine formation at 10  $\mu$ M,  $\alpha$ -MSH (11-13) (SEQ ID NO: 3) was most effective at 1  $\mu$ M, and ACTH (1-24) (SEQ ID NO: 12) was most effective ... of cells with  $\alpha$ -MSH(1-13) (SEQ ID NO: 3) or  $\alpha$ -MSH(11-13) (SEQ ID NO: 1) prior to treatment ... produce  $\alpha$ -MSH (SEQ ID NO: 1) naturally ...

[0133] ... Both  $\alpha$ -MSH(1-13) (SEQ ID NO: 3) and  $\alpha$ -MSH(11-13) (SEQ ID NO: 3) induced cAMP accumulation at concentrations as low as 1  $\mu$ m.  $\alpha$ -MSH(1-13) (SEQ ID NO: 1) exhibiting its strongest effect at 10  $\mu$ M, while  $\alpha$ -MSH(11-13) (SEQ ID NO: 3) exhibited its strongest effect at 50  $\mu$ M. ...accumulation.  $\alpha$ -MSH(1-13) (SEQ ID NO: 3) was the more effective of the two  $\alpha$ -MSH peptides, but  $\alpha$ -MSH(11-13) (SEQ ID NO: 1) was ...

[0134] ... effects of KPV (SEQ ID NO: 1) and the KPV dimer (also referred to as (CKPV)<sub>2</sub>) (SEQ ID NO: 4) in reducing edema ... Saline control (31), (CKPV)<sub>2</sub> (SEQ ID NO: 4) 0,5 mg/Kg (7), (CKPV)<sub>2</sub> (SEQ ID NO: 4) 1,25 mg/Kg (7), (CKPV)<sub>2</sub> (SEQ ID NO: 4) 2,5 mg/Kg (16), (CKPV)<sub>2</sub> (SEQ ID NO: 4) 5,0 mg/Kg (17), (CKPV)<sub>2</sub> (SEQ ID NO: 4) 7,5 mg/Kg (17), KPV (SEQ ID NO: 4) 2,5 mg/Kg (9), KPV (SEQ ID NO: 1) 5,0 mg/Kg (17), KPV (SEQ ID NO: 1) 7,5 mg/Kg (24) and prednisolone suc.

100 mg/Kg (17)...dosages of (CKPV)<sub>2</sub> (SEQ ID NO: 4) at 1.25 mg/Kg, 2.5 mg/Kg, 5.0 mg/Kg, and 7.5 mg/Kg and the dosage of KPV (SEQ ID NO: 1) ...